## REMARKS

# Status of the Claims

Claims 50-78 are pending in this application. Claims 50-78 stand rejected.

## The Office Action

## The §103(a) Rejection

The Examiner has rejected claims 50-57, 63, 64, 68, and 76-78 under 35 U.S.C. §103(a) as being unpatentable over WO 2001/42216 ("the '216 application). The Examiner contends that "it would have been obvious to one of ordinary skill in the art to replace the hydrogen substituent of the prior art for an alkyl substituent of the instantly claimed compound." The Examiner further contends that "[t]he modification of one radical for another does not modify the pharmacological behavior of the compounds." Applicants traverse.

Applicants respectfully submit that the Examiner has not made a prima facie case for obviousness. Contrary to the Examiner's assertion, the compounds of the instant claims have an improved ability, relative to the corresponding drug, of crossing the blood brain barrier (see page 5, paragraph [0015]). Typically, caspase inhibitors are characterized by undesirable pharmacological properties due to their peptidic nature. They are charged at physiological pH, which inhibits their ability to cross the blood brain barrier and to penetrate cells at therapeutically useful levels (see, pages 2-3 in the specification). In the present case, the addition of an alkyl group modifies the pharmacological behavior of the acid compounds by improving blood brain barrier penetration. Moreover, these compounds have the ability to undergo cleavage and provide caspase inhibitors within the brain. Accordingly, the compounds of the instant application are surprising effective as caspase inhibitors prodrugs for crossing the blood brain barrier.

In view of the arguments above, applicants respectfully request that the Examiner withdraw this §103(a) rejection.

## The Non-statutory Double Patenting Rejection

The Examiner has <u>provisionally</u> rejected claims 50-76 and 78 as being unpatentable in view of co-pending Application No., 10/609,147. The Examiner contends that

"although the conflicting claims are not identical, they are not patentably distinct from each other because the claimed subject matter is an obvious variant." Applicants traverse.

As discussed above, applicants do not consider the ester, amide, and hydroxamide prodrugs to be obvious variants of the corresponding acids. Nevertheless, solely to expedite prosecution, applicants stand ready to consider terminal disclaimers to overcome these obviousness-type double patenting rejections upon allowance of the rejected claims.

### CONCLUSION

Accordingly, applicants request that the Examiner considers the foregoing remarks, and allow the pending claims to issue. If the Examiner believes that a telephone discussion would further issuance of this application, the Examiner is invited to call the undersigned attorney or agent at any time.

Respectfully submitted,

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